Reconstitution of the expression unit composed by the long λ pL promoter (useful for Nalidixic acid induction) and the CLYTA-Mage-1 coding sequence pRIT14614):

A EcoRI-NCO_1 restriction fragment containing the long PL promoter and a part of CLYTA sequences was prepared from plasmid pRIT DVA6 and inserted between the EcoRI-NCO_1 sites of plasmid pRIT14613.

The recombinant plasmid pRIT14614 was obtained.

The recombinant plasmid pRIT14614 (see figure 17) encoding the fusion protein CLYTA-Mage-1-His was used to transform E. coli AR120. A Kan resistant candidate strain was selected and characterized.

Characterization of the recombinant protein:

Bacteria were grown on LB Medium supplemented with 50mg/ ml kanamycin at 30 °C. When the culture had reached 0D≈ 400 (at 620nm) Nalidixic acid was added to a final concentration of 60 mg/ ml.

After 4 hours induction, cells were harvested, resuspended in PBS and lysed by desintegration (disintegration CLS "one shot" type). After centrifugation, pellet supernatant and total extract were analyzed by SDS-PAGE. Proteins were visualized in Coomassie Bleu stained gels, where the fusion protein represented about 1 % of the total E. coli proteins. The fusion protein was identified by Western blot analysis using rabbits anti-Mage-1 polyclonal antibodies. The recombinant protein appeared as a single band with an apparent MW of about 49 kD.

EXAMPLE X:
CLYTA - MAGE-3-HIS

A: Tumour rejection recombinant antigen: a fusion protein CLYTA -Mage-3-His where the C-lyt A fusion partner lead to expression of a soluble protein, act as affinity tag and provides a useful T-helper.

Preparation of the E. coli strain expressing a fusion protein CLYTA-Mage-3-His tail

Construction of the expression plasmid pRIT14646 and transformation of the host strain AR 120:

Protein design:
The design of the fusion protein Clyta-Mage-3-His to be expressed in E. coli is described in figure 18.

The primary structure of the resulting protein has the sequence described in SEQUENCE ID No.9: and the coding sequence in sequence ID No. 10

The coding sequence corresponding to the above protein design was placed under the control of λ pL promoter in a E. coli expression plasmid.

Cloning:

The starting material was **the vector PCUZ1** that contains the 117 C-terminal codons of the LytA coding region from Streptococcus pneumoniae, described in Gene 43, (1986) p. 265-272 and **the vector pRIT14426,** in which we have previously subcloned the MAGE-3 gene cDNA from a plasmid received from Dr Tierry Boon from the Ludwig Institute.

The cloning strategy for the expression of CLYTA-MAGE-3-His protein (see outline in Figure 19) included the following steps:

1- Preparation of the CLYTA-MAGE-3-His coding sequence module:

1.1. The first step was a PCR amplification, destined to flank the CLYTA sequences with the AflII and AflIII restriction sites. The PCR amplification was done using the plasmid **PCUZ1**as template and as primers the oligonucleotide sense: 5' tta aac cac acc tta agg agg ata taa cat atg aaa ggg gga att gta cat tca gac , and the oligonucleotide antisense: 5' ccc aca tgt cca gac tgc tgg cca att ctg gcc tgt ctg cca gtg . This leads to the amplification of a 427 nucleotides long CLYTA sequence. The above amplified fragment was cloned into the TA cloning vector of Invitrogen to get the intermediate vector pRIT14661

1.2. The second step was linking of CLYTA sequences to the MAGE-3-His sequences, to generate the coding sequence for the fusion protein. This step included the excision of a Afl II-Afl-III Clyta fragment and insertion into the vector pRIT14426 previously opened by Afl IIand NcoI (NcoI and AflII compatible) restriction enzymes and gave rise to the plasmid pRIT14662.

2.- Reconstitution of the expression unit composed by the long λ pL promoter (useful for Nalidixic acid induction) and the CLYTA-Mage-3 coding sequence:

A BglII - XbaI restriction fragment containing the short pL promoter and the CLYTA-Mage-3-His coding sequences was prepared from plasmid pRIT14662. and inserted between the BglII - XbaI sites of plasmid TCM67 (a pBR322 derivative containing the resistance to ampicillin, and the long λ pL promoter, described in the international application PCT/EP92/O1827). The plasmid pRIT14607 was obtained.

The recombinant plasmid pRIT14607 encoding the fusion protein ***Clyta-Mage-3 His*** was used to transform E. coli AR 120 (Mott et al.1985, Proc. Natl. Acad. Sci, 82: 88). An ampicillin resistant candidate strain was selected and characterized.

3. Preparation of plasmid pRIT 14646:

Finally a plasmid similar to pRIT 14607 but having the Kanamycin selection was constructed (pRIT 14646)

Characterization of the recombinant protein:

Bacteria were grown on LB Medium supplemented with 50mg/ ml kanamycin at 30°C. When the culture had reached 0D= 400 (at 600nm) Nalidixic acid was added to a final concentration of 60?g/ ml.

After 4 hours induction , cells were harvested, resuspended in PBS and lysed by desintegration (desintegration CLS "one shot" type). After centrifugation, pellet supernatant and total extract were analyzed by SDS-PAGE. Proteins were visualized in Coomassie Bleu stained gels, where the fusion protein represented about 1% of the total E. coli proteins. The fusion protein was identified by Western blot analysis using rabbits anti-Mage-3 polyclonal antibodies . The recombinant protein appeared as a single band with an apparent MW of about 58 kD.

EXAMPLE XI:

Purification of the recombinant protein CLYTA-Mage-3 His:

The recombinant bacteria AR120 (pRIT 14646) were grown in a 20 Litters fermentor under fed-batch conditions at 30°. The expression of the recombinant protein was induced by adding Nalidixic acid at a final concentration of 60 ?g/ml. Cells were harvested at the end of fermentationand and lyzed at 60 OD/600 by two passages through a French Press disrupter (20 000 psi). Lysed cells were pelleted 20 min at 15 000 g at 4 °C. Supernatant containing the recombinant protein was loaded onto exchange DEAE Sepharose CL6B resin (Pharmacia) pre-equilibrated in 0.3M NaCl, 20 mM Tris HCl pH 7.6 Buffer A. After a column wash with buffer A, fusion protein was eluted by 2 % choline in (Buffer A). Positive antigen

fractions, as revealed by Western blotting analysis using an anti Mage-3 antibody, were pooled. DEAE-eluted antigen was brought to 0.5 % Empigen BB (a zwitterionic detergent) and to 0.5 M NaCl before loading onto an Ion Metal Affinity chromatography column preequilibrated in 0.5 % Empigen BB, 0.5 M NaCl, 50 mM phosphate buffer pH 7.6 (Buffer B).

IMAC column was washed with buffer B until 280 nm absorbency reached the base line. A second wash in buffer B without Empigen BB (Buffer C) in order to eliminate the detergent was executed before Antigen elution by an Imidazole gradient 0-250mM Imidazole in buffer C.

0.090-0.250 M Imidazole fractions were pooled, concentrated on a 10 kDa Filtron omega membrane before dialysis versus PBS buffer.

CONCLUSION:

We have demonstrated that the fused protein LPD-MAGE3-His is immunogenic in mice, and that this immunogenicity (the proliferative response and antibody response) can be further increased by the use of the adjuvant described above. Purification can be enhanced by derivatising the thiols that form disulphide bonds.

We have also demonstrated that a better antibody response was triggered by the vaccination with the LPD-MAGE-3-His in the presence of the adjuvant. The predominant isotype found in the serum of C57BL/6 being IgG2b suggesting that a TH1 type immune response was raised.

In the human, clinical setting a patient treated with LPD-MAGE3-His in an unadjuvanted formulation was cleared of melanoma.

CLAIMS:

1. A tumour-associated antigen derivative from the MAGE family.

2. An antigen as claimed in claim 1, when the derivative is a MAGE protein linked to an immunological fusion or expression enhancer partner.

3. An antigen as claimed in claim 1 or 2 wherein the derivative comprises an affinity tag.

4. An antigen as claimed in any of claims 1 to 3 which contains a derivatised free thiol.

5. An antigen as claimed in claim 4 which is a carboxyamide or carboxymethylated derivative.

6. A protein as claimed in claim 2, 3, 4 or 5 wherein the fusion partner is protein D or fragment thereof from Heamophilus influenzae B, NS1 protein from influenza or a fragment thereof or Lyta from Streptococcus pneumoniae or fragment thereof.

7. A protein as claimed in claim 2, 3, 4 or 5 wherein the fusion partner is the lipidated form of protein D or fragment thereof from Heamophilus influenza B.

8. A protein as claimed in claim 1 to 7 wherein the MAGE protein is selected from the group MAGE A1, MAGE A2, MAGE A3, MAGE A4, MAGE A5, MAGE A6, MAGE A7, MAGE A8, MAGE A9, MAGE A10, MAGE A11, MAGE A12, MAGE B1, MAGE B2, MAGE B3 and MAGE B4, MAGE C1, MAGE C2.

9. A nucleic acid sequence encoding a protein as claimed herein.

10. A vector comprising a nucleic acid of claim 9.

11. A host transformed with a vector of claim 10.

12. A vaccine containing a protein as claimed in any of claims 1 to 8 or a nucleic acid as claimed in claim 9.

13. A vaccine as claimed in claim 12 additionally comprising an adjuvant, and/or immunostimulatory cytokine or chemokine.

14. A vaccine as claimed in claim 12 or 13 wherein the protein is presented in an oil in water or a water in oil emulsion vehicle.

15. A vaccine as claimed in claim 13 or 14 wherein the adjuvant comprises 3D-MPL, QS21 or a CpG oligonucleotide.

16. A vaccine as claimed herein additionally comprising one or more other antigens.

17. A vaccine as claimed herein for use in medicine.

18. Use of a protein or nucleic acid as claimed herein for the manufacture of a vaccine for immunotherapeutically treating a patient suffering from melanomas or other MAGE-associated tumours.

19. A process for the purification of a MAGE protein or derivative thereof, comprising reducing the disulphide bonds, blocking the resulting free thiol group with a blocking group, and subjecting the resulting derivative to one or more chromatographic purification steps.

20. A process for the production of a vaccine, comprising the steps of purifying a MAGE protein or a derivative thereof, by the process of claim 19 and formulating the resulting protein as a vaccine.

Figure 1 : LPD-MAGE-3-His

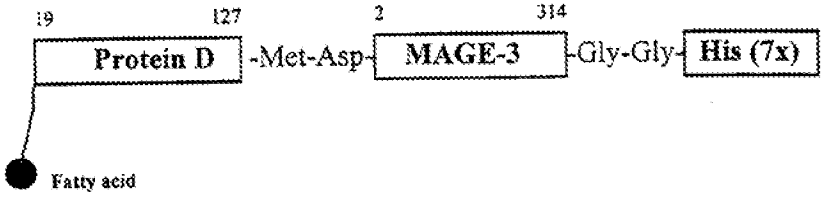

FIGURE 2 : Construction of the expression vectorpRIT 14586

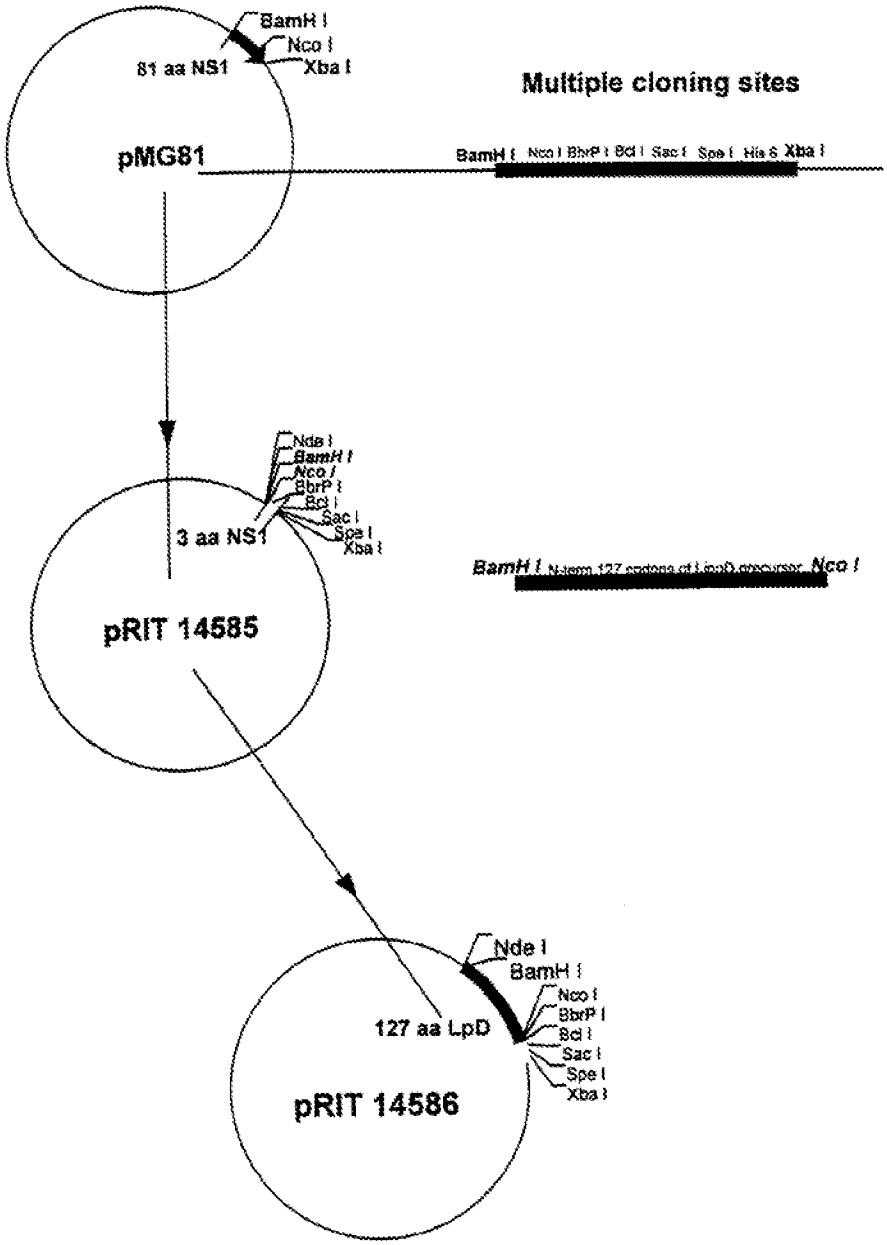

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FIGURE 3 : Construction of plasmid pRIT 14477 expressing the fusion protein Prot. D 1/3-MAGE-3-His tail

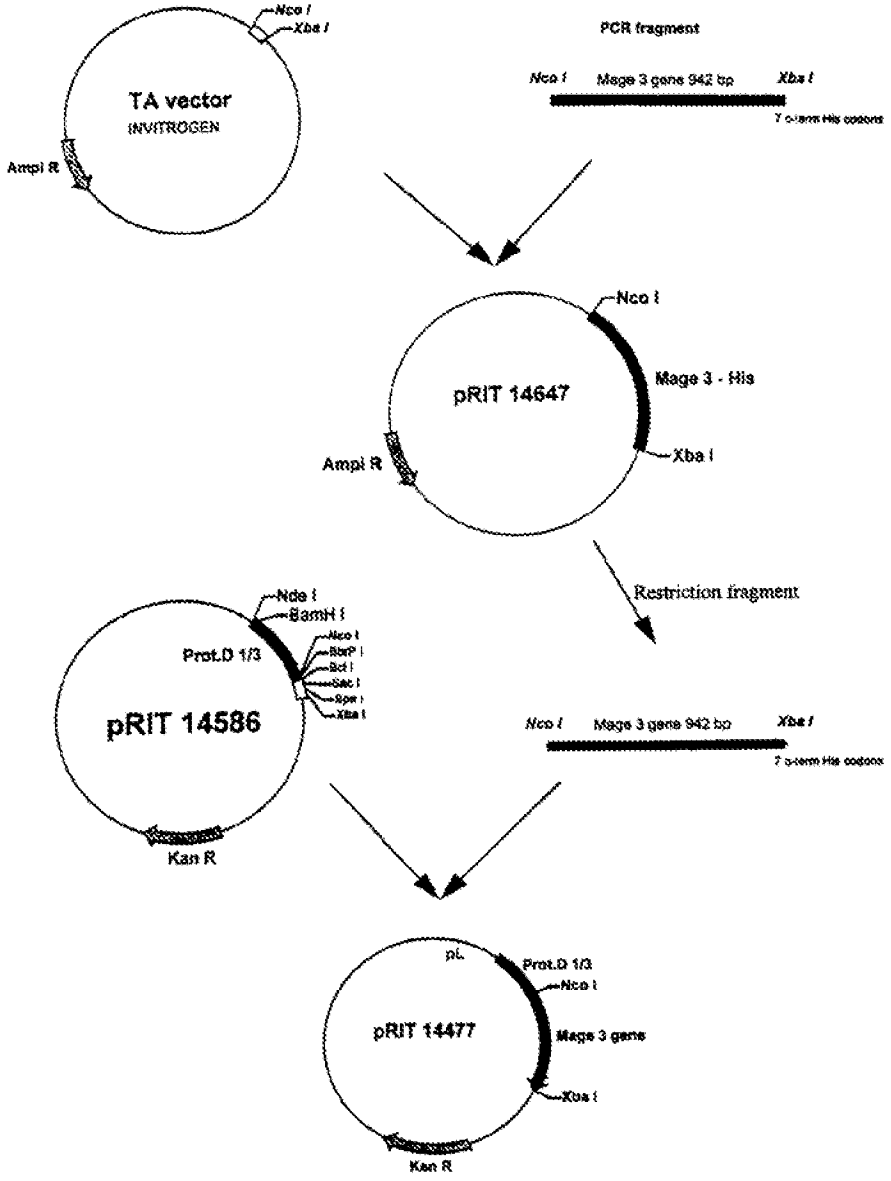
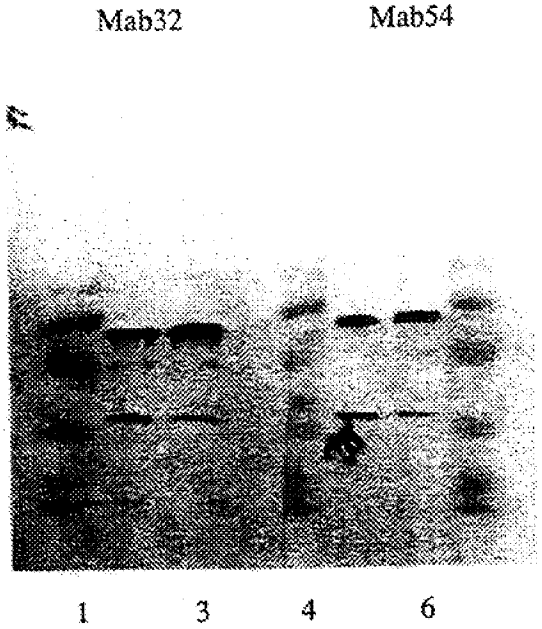


FIGURE 4 Western blot analysis of LPD-MAGE-3-His protein Anti-MAGE-3 monoclonal antibodies Mab 32 and Mab 54



1, 4, and 7 : molecular weight
2 : lot 96K19 revealed with Mab 32
3 : lot 96J22 revealed with Mab 32
4 : lot 96K19 revealed with Mab 54
5 : lot 96J22 revealed with Mab 54

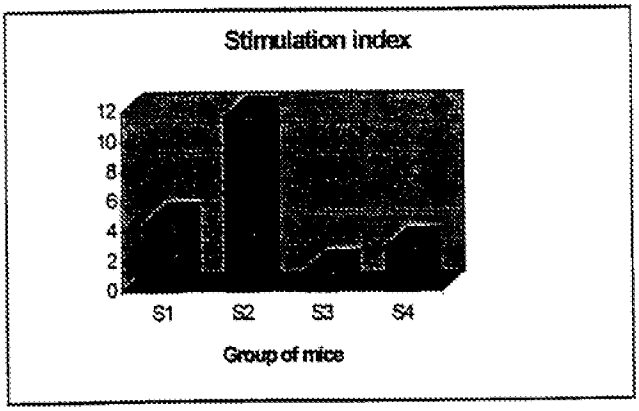
Figure 5

IMMUNOGENICITY OF MAGE 3 IN MICE (C57BL6)

Lymphoproliferation on spleen cells.

72Hrs stimulation with 0.1μg/ml His Mage 3 on μbeads

Groups of mice		3H Thymidine incorporation baseline (CPM): 0.1 μg/ml μbeads
S1	Non formulated LipoD Mage3 His	1284
S2	LipoD Mage3 His + SBAS2	679
S3	SBAS2	805
S4	medium	1242



5

FIGURE 6:

IMMUNOGENICITY OF MAGE 3 IN MICE (C57BL/6)

Lymphoproliferation on lymph node cells.

72Hrs stimulation with 1μg/ml His Mage 3 on μbeads

Groups of mice		3H Thymidine incorporation baseline (CPM): 1 μg/ml μbeads
LN1	Non formulated LipoD Mage3 His	477
LN2	LipoD Mage3 His + SBAS2	1025
LN3	SBAS2	251
LN4	medium	110

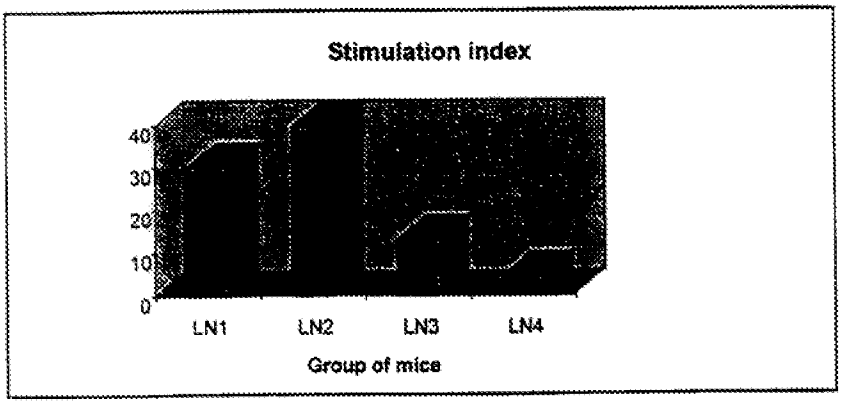


FIGURE 7:

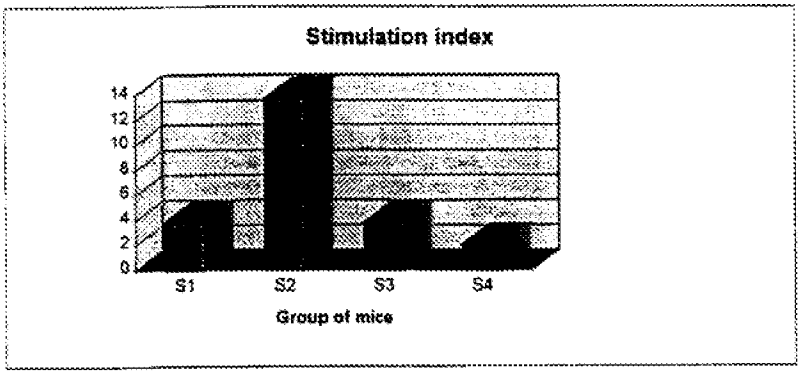
IMMUNOGENICITY OF MAGE3 IN MICE (BalbC)

Lymphoproliferation on spleen cells

72Hrs stimulation with 0.1µg/ml His Mage3 (A)
His Mage 3 coated on µbeads (B)

Groups of mice		3H Thymidine incorporation :cpm	
		none	0.1µg/ml µb
S1	Non Formulated LipoD Mage3 His	1002	1329
S2	LipoD Mage 3 His + SBAS2	1738	4997
S3	SBAS2	1685	3393
S4	Medium	1535	1129

A



B

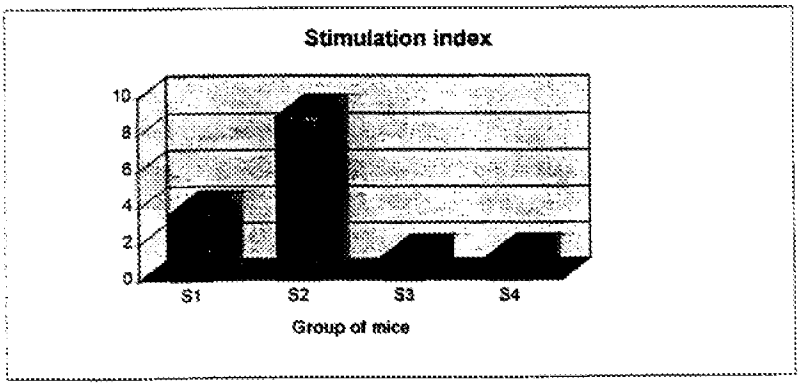


FIGURE 8:

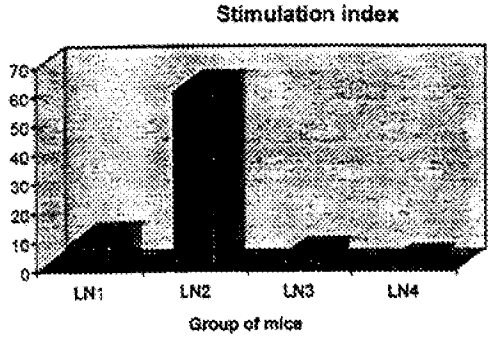
IMMUNOGENICITY OF MAGE3 IN MICE (BalbC)

Lymphoproliferation on popliteal lymph node cells

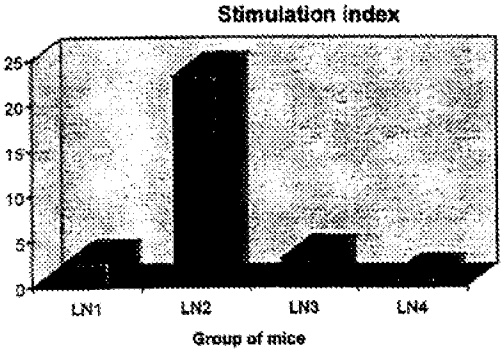
72Hrs stimulation with 1 µg/ml His Mage 3 (A)
His Mage 3 coated on µbeads(B)

Groups of mice		3H Thymidine incorporation :cpm none	1µg/ml µb
LN1	Non Formulated LipoD Mage3 His	309	386
LN2	LipoD Mage 3 His + SBAS2	438	410
LN3	SBAS2	522	637
LN4	Medium	318	399

A

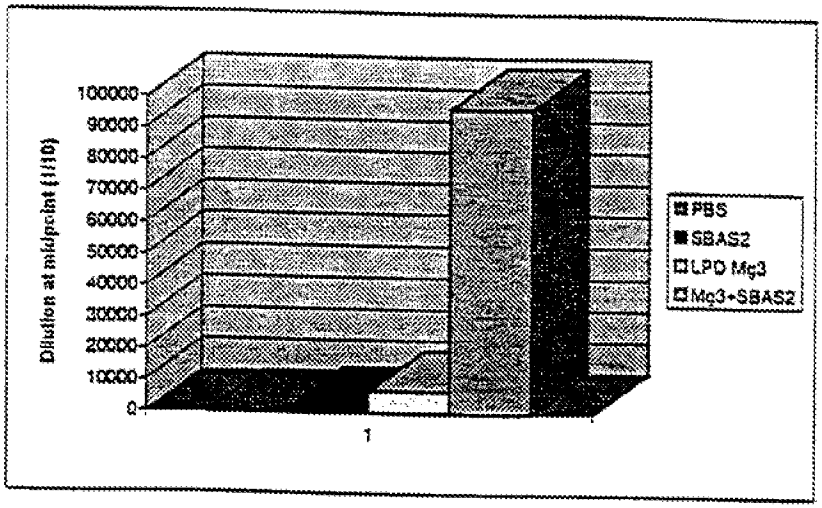


B

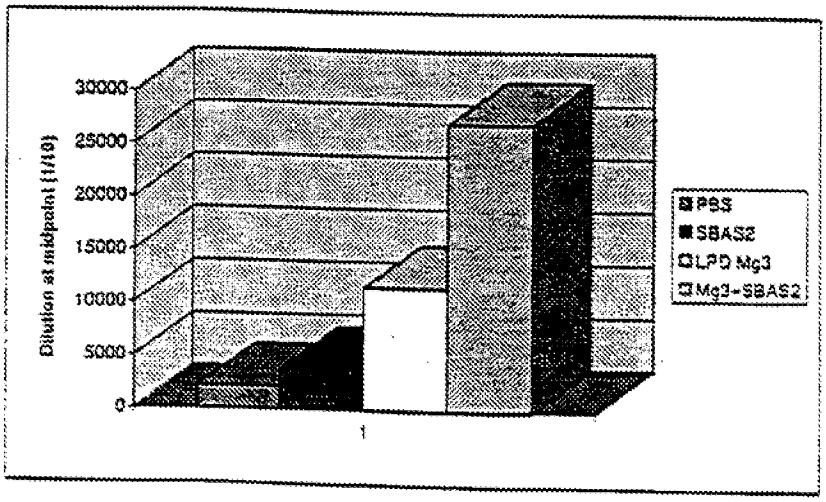


Anti-Mage3 antibodies in the serum of mice immunized with LipoD Mage3 His in SBAS2 or not

BALB C mice

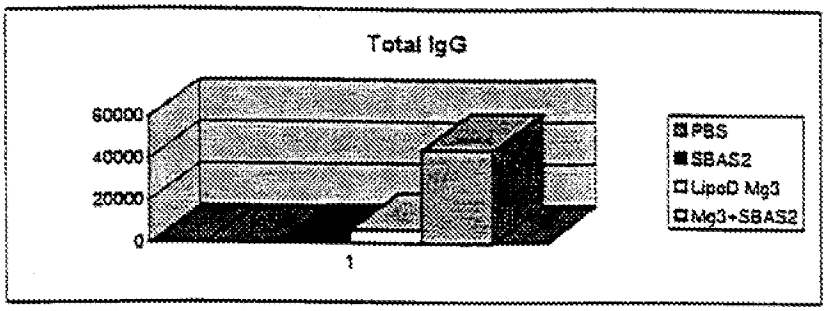


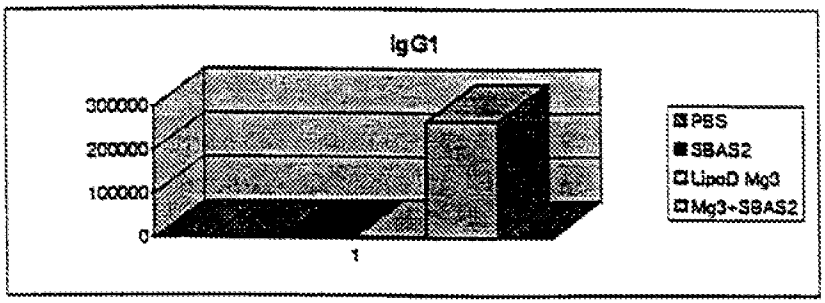
C57BL/6 mice

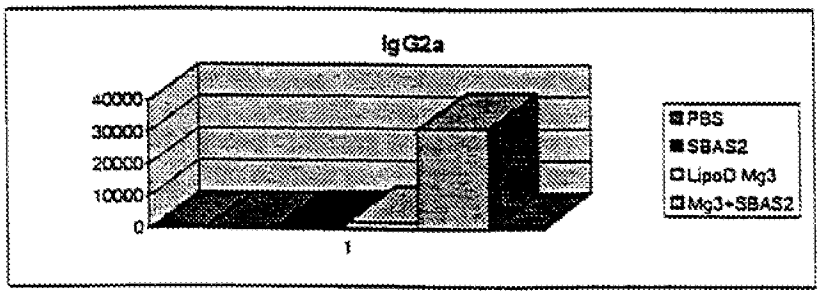


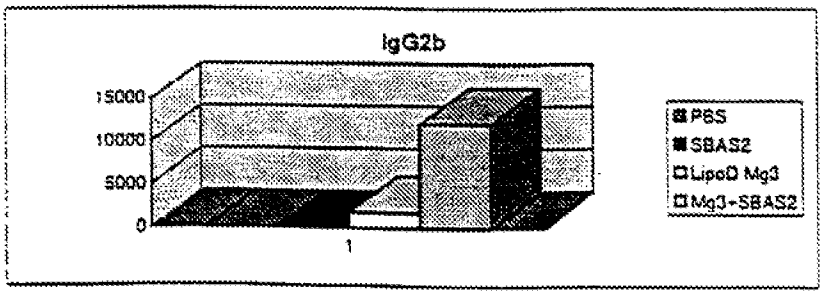
Subclass-specific antibody responses in Balb/c mice

	Tot. IgG	IgG1	IgG2a	IgG2b	IgA	IgM
PBS	0	0	0	0	0	0
SBAS2	733	719	378	11	0	0
LPD Mg3 His	6182	2049	2058	1835	0	0
LPD Mg3 H /SBAS2	44321	267884	31325	12160	0	0



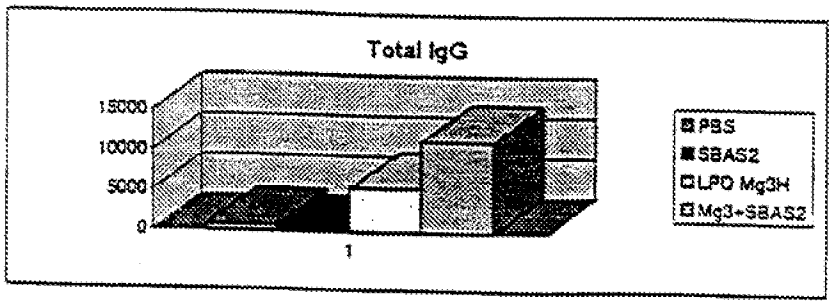


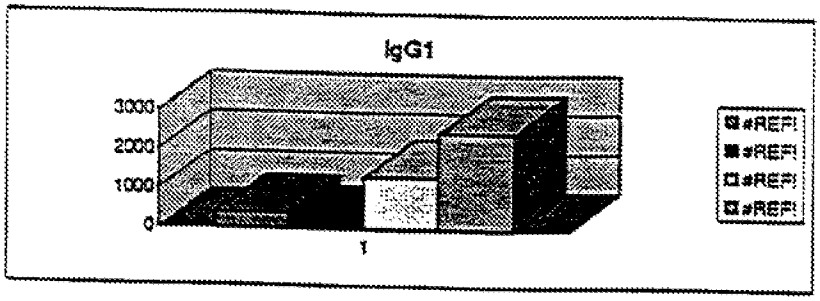


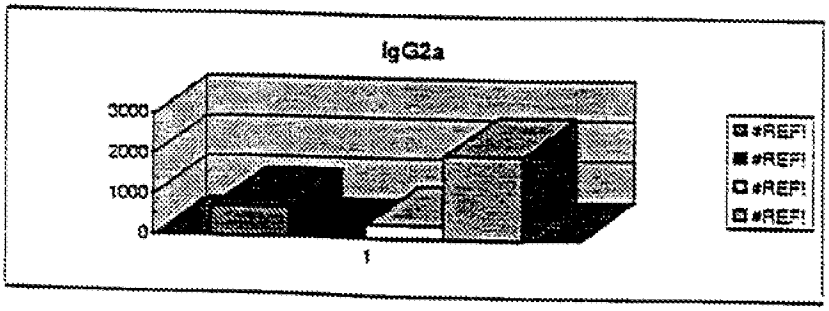


Subclass-specific antibody responses in C57BL/6 mice

	Total IgG	IgG1	IgG2a	IgG2b	IgA	IgM
PBS	807	405	718	22.8	2.8	33.8
SBAS2	37	137	0	0	0	19
LPO Mg3His	5471	1343	332	4540	135	5
LPO Mg3H/SBAS2	11489	2477	2070	8118	55	46







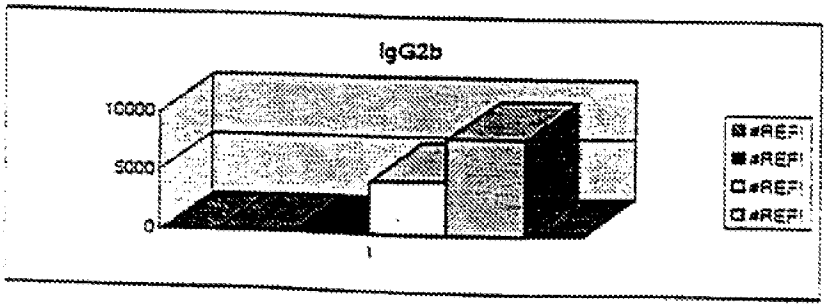


Figure 12

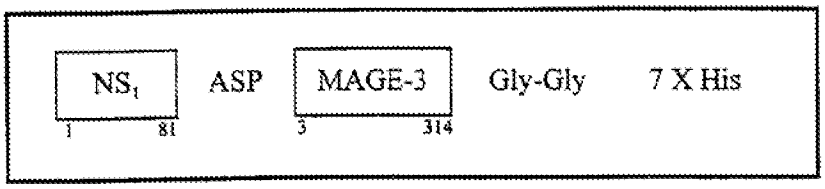


Figure 13

Construction of plasmid pRIT14426

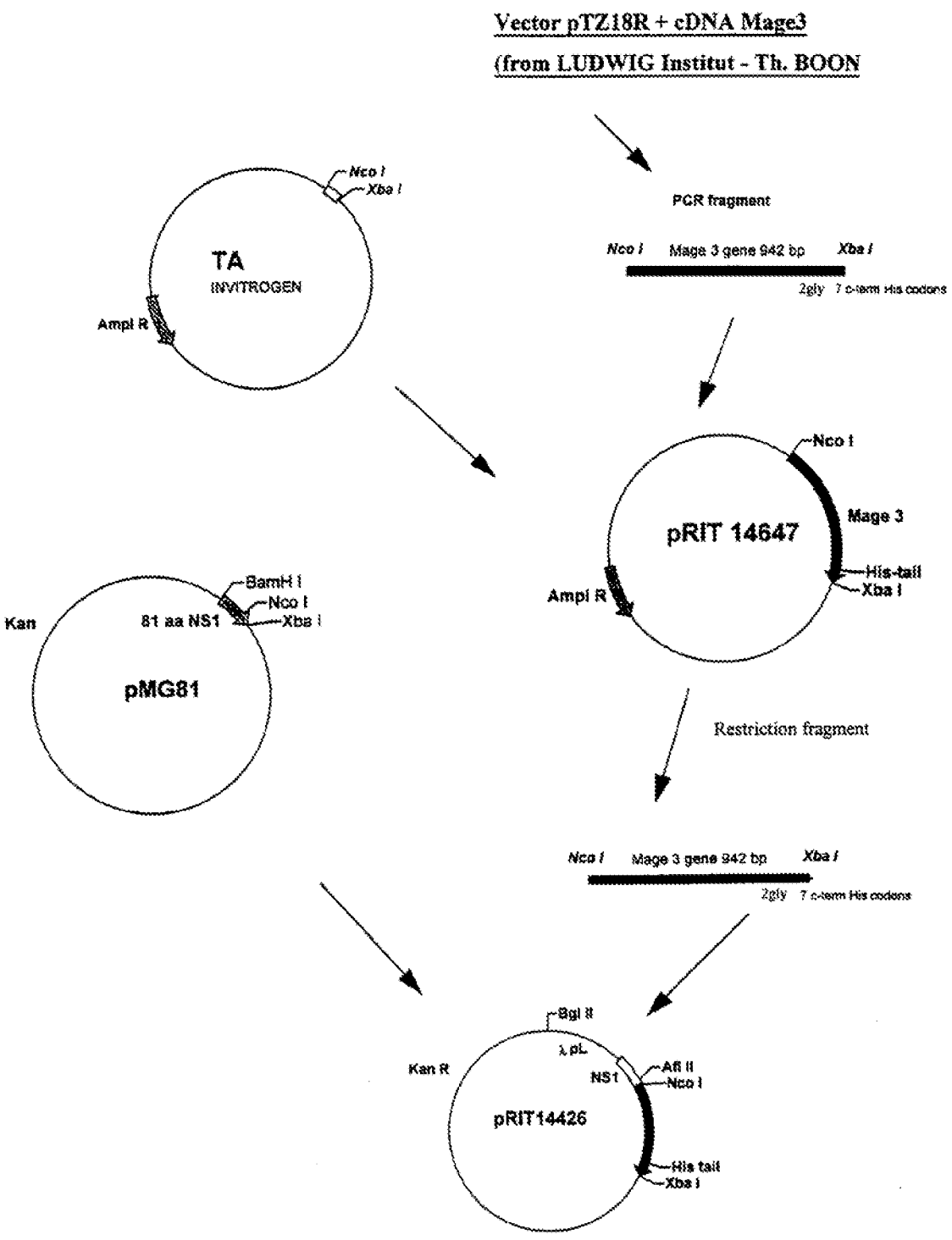
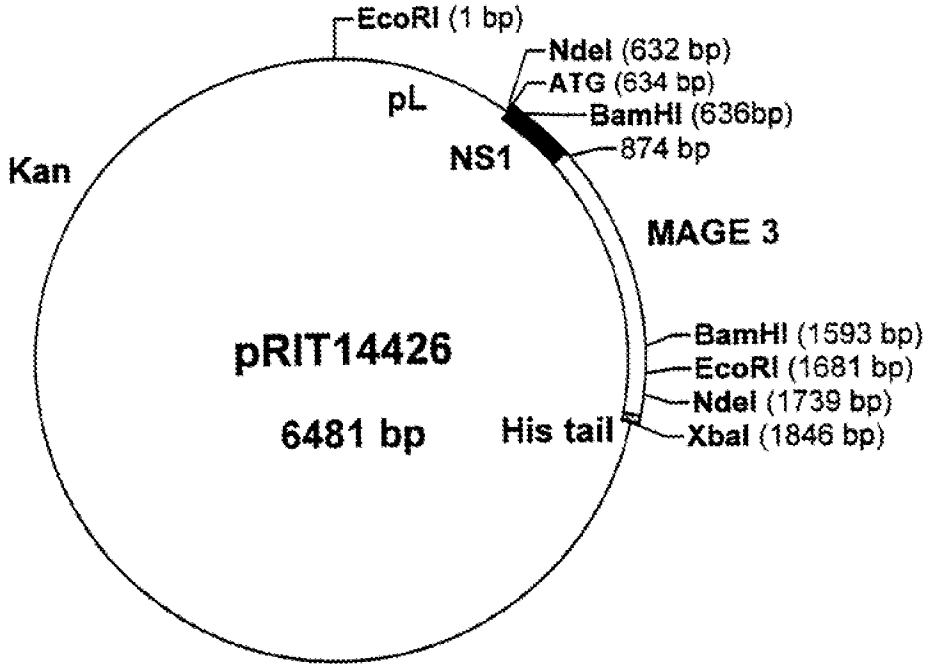


Figure 14:

Plasmid map of pRIT14426



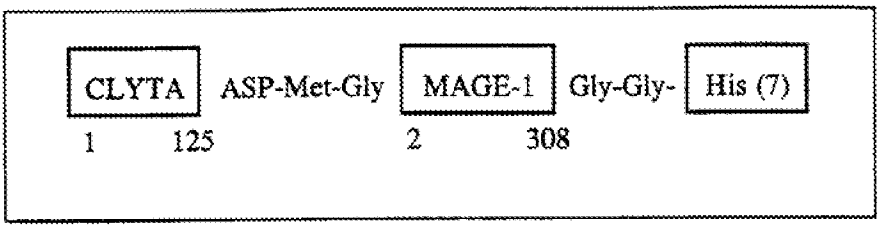

CLYTA
ASP-Met-Gly
MAGE-1
Gly-Gly-
His (7)
1
125
2
308

Figure 16 : construction of plasmid pRIT 14613.

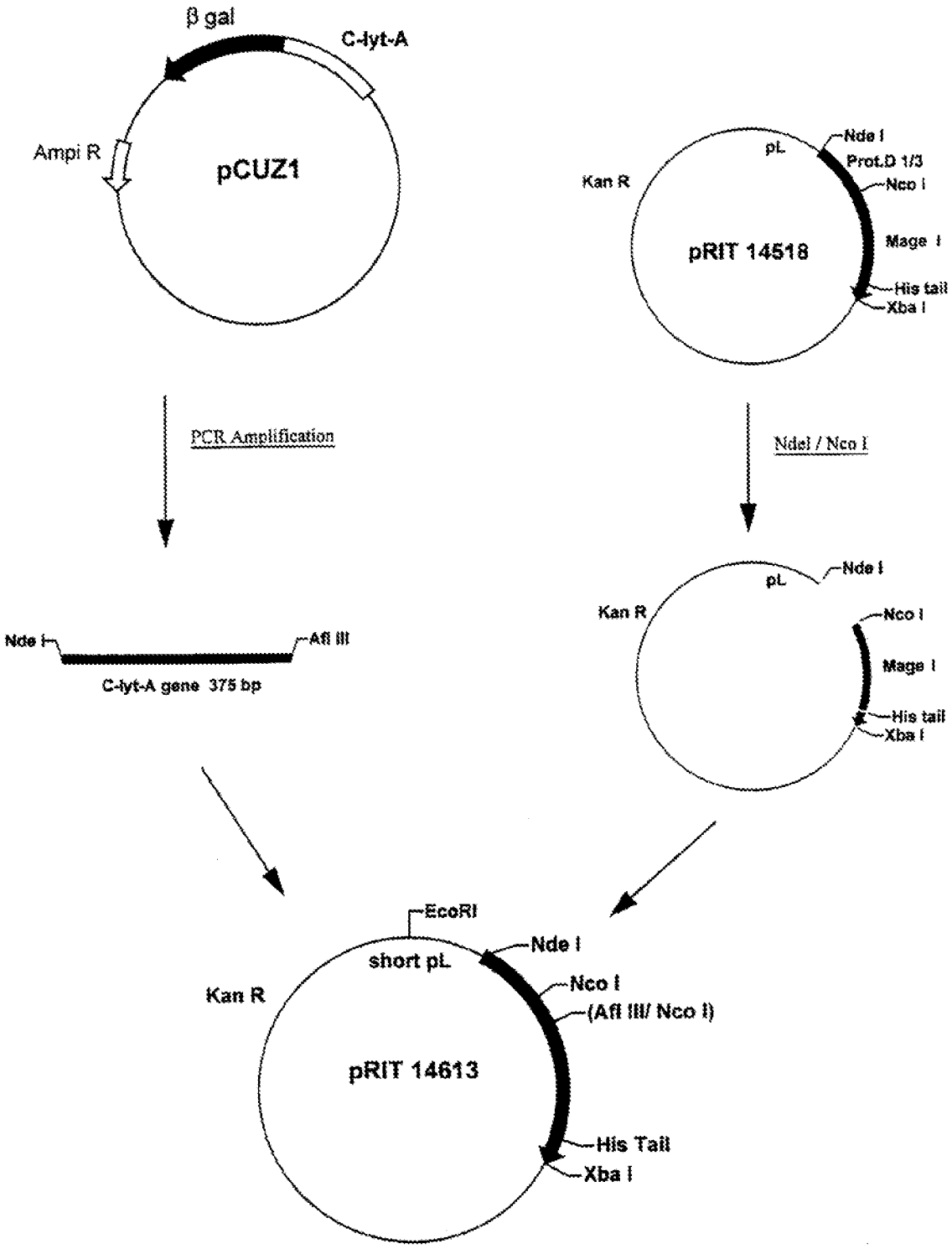


Figure 17 construction of plasmid pRIT 14614

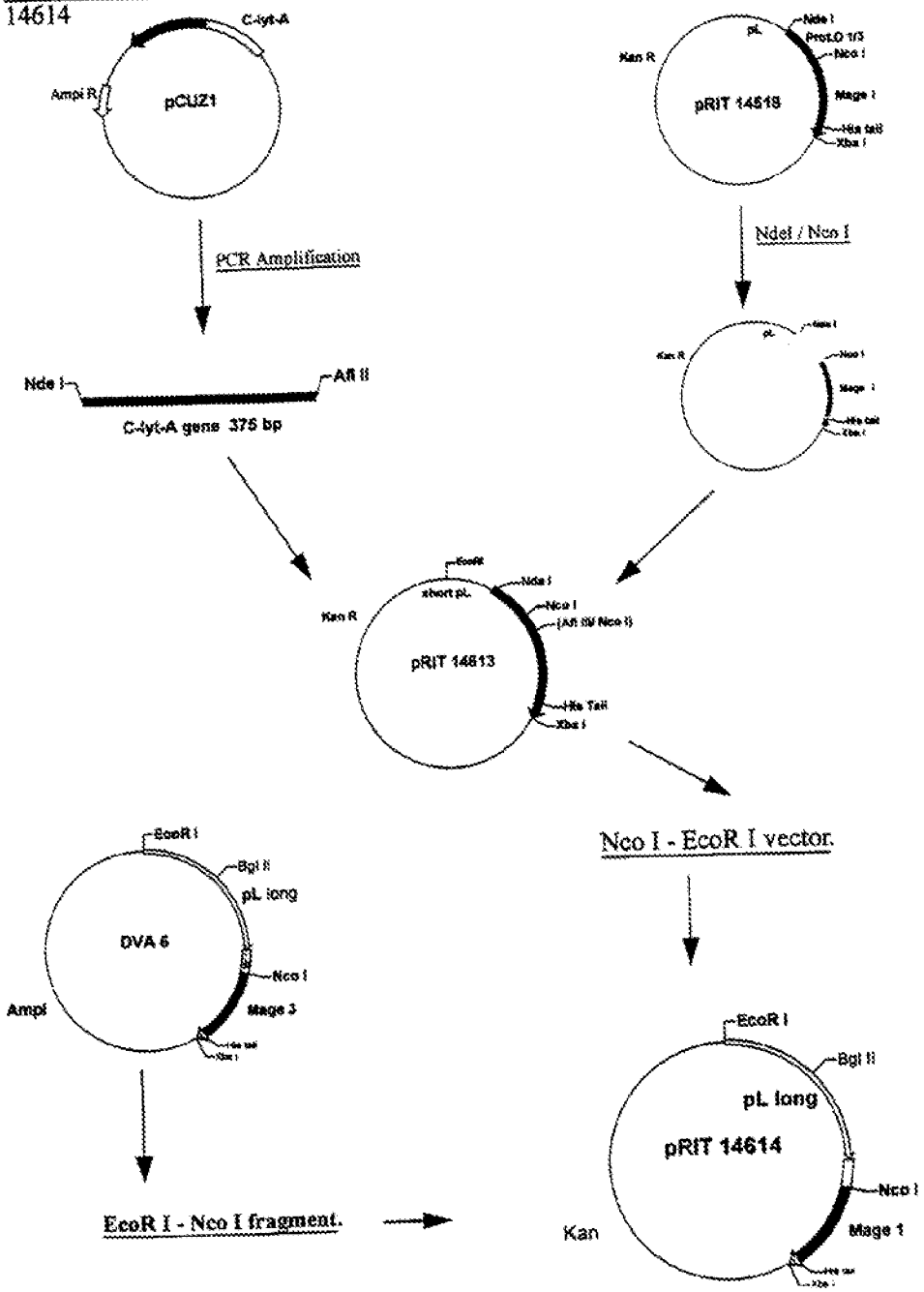


Figure-18

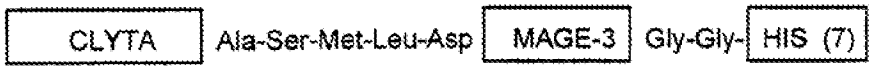
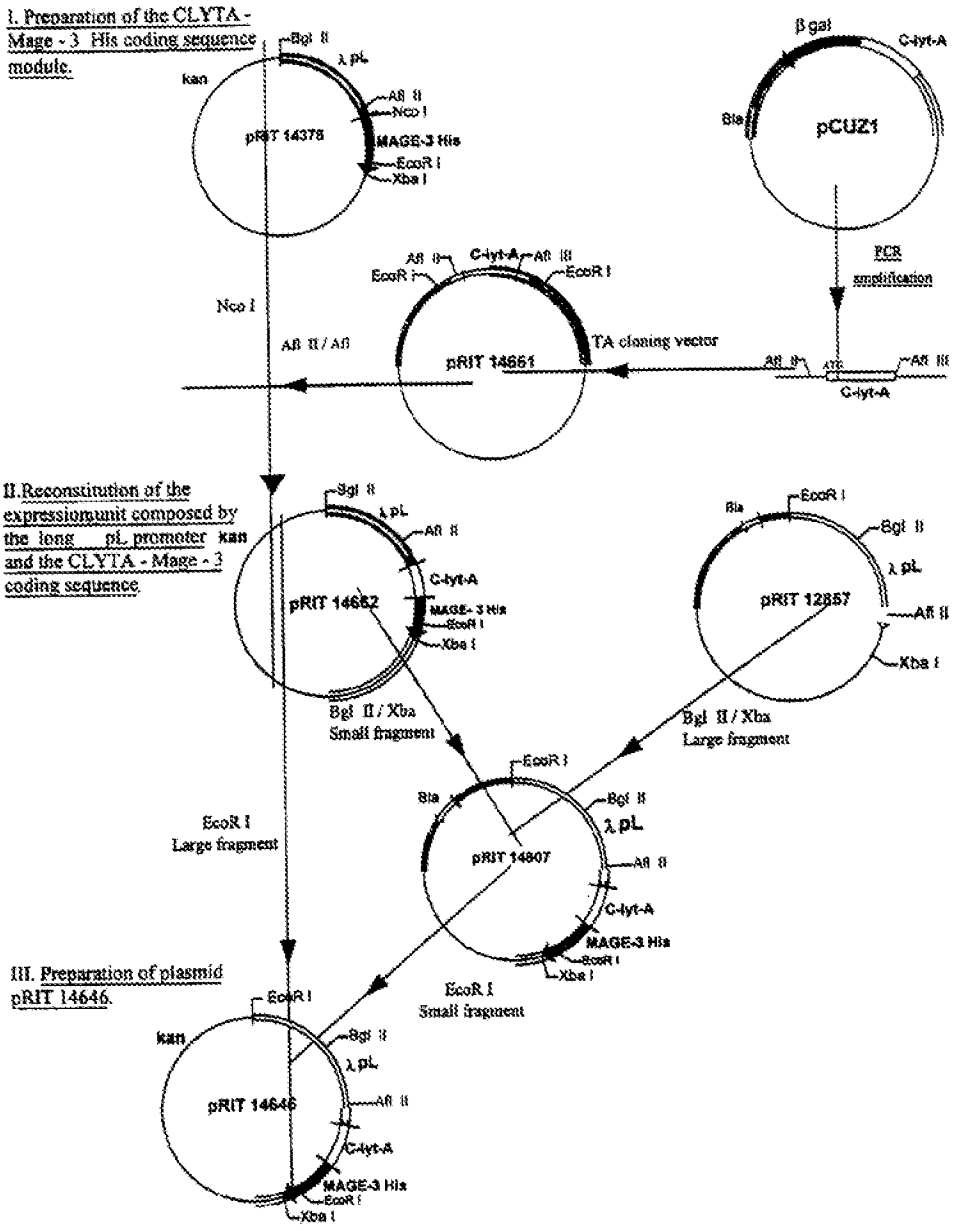


Figure 19

FIGURE 19 : Construction of plasmid pRIT 14646



SEQUENCE LISTING

(1) GENERAL INFORMATION

(i) APPLICANT: SmithKline Beecham Biologicals

(ii) TITLE OF THE INVENTION: Vaccine

(iii) NUMBER OF SEQUENCES: 10

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: SmithKline Beecham
(B) STREET: 2 New Horizons Court, Great West Road, B
(C) CITY: Middx
(D) STATE:
(E) COUNTRY: UK
(F) ZIP: TW8 9EP

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Diskette
(B) COMPUTER: IBM Compatible
(C) OPERATING SYSTEM: DOS
(D) SOFTWARE: FastSEQ for Windows Version 2.0

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:

(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Dalton, Marcus J
(B) REGISTRATION NUMBER:
(C) REFERENCE/DOCKET NUMBER: B45126

(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: 0181 9756348
(B) TELEFAX: 0181 9756177
(C) TELEX:

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 452 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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 1               5                  10                  15
Ala Gly Cys Ser Ser His Ser Ser Asn Met Ala Asn Thr Gln Met Lys
            20                  25                  30
Ser Asp Lys Ile Ile Ile Ala His Arg Gly Ala Ser Gly Tyr Leu Pro
```

```
          35                  40                  45
Glu His Thr Leu Glu Ser Lys Ala Leu Ala Phe Ala Gln Gln Ala Asp
      50                  55                  60
Tyr Leu Glu Gln Asp Leu Ala Met Thr Lys Asp Gly Arg Leu Val Val
65                  70                  75                  80
Ile His Asp His Phe Leu Asp Gly Leu Thr Asp Val Ala Lys Lys Phe
                85                  90                  95
Pro His Arg His Arg Lys Asp Gly Arg Tyr Tyr Val Ile Asp Phe Thr
            100                 105                 110
Leu Lys Glu Ile Gln Ser Leu Glu Met Thr Glu Asn Phe Glu Thr Met
        115                 120                 125
Asp Leu Glu Gln Arg Ser Gln His Cys Lys Pro Glu Glu Gly Leu Glu
    130                 135                 140
Ala Arg Gly Glu Ala Leu Gly Leu Val Gly Ala Gln Ala Pro Ala Thr
145                 150                 155                 160
Glu Glu Gln Glu Ala Ala Ser Ser Ser Ser Thr Leu Val Glu Val Thr
                165                 170                 175
Leu Gly Glu Val Pro Ala Ala Glu Ser Pro Asp Pro Pro Gln Ser Pro
            180                 185                 190
Gln Gly Ala Ser Ser Leu Pro Thr Thr Met Asn Tyr Pro Leu Trp Ser
        195                 200                 205
Gln Ser Tyr Glu Asp Ser Ser Asn Gln Glu Glu Glu Gly Pro Ser Thr
    210                 215                 220
Phe Pro Asp Leu Glu Ser Glu Phe Gln Ala Ala Leu Ser Arg Lys Val
225                 230                 235                 240
Ala Glu Leu Val His Phe Leu Leu Leu Lys Tyr Arg Ala Arg Glu Pro
                245                 250                 255
Val Thr Lys Ala Glu Met Leu Gly Ser Val Val Gly Asn Trp Gln Tyr
            260                 265                 270
Phe Phe Pro Val Ile Phe Ser Lys Ala Ser Ser Ser Leu Gln Leu Val
        275                 280                 285
Phe Gly Ile Glu Leu Met Glu Val Asp Pro Ile Gly His Leu Tyr Ile
    290                 295                 300
Phe Ala Thr Cys Leu Gly Leu Ser Tyr Asp Gly Leu Leu Gly Asp Asn
305                 310                 315                 320
Gln Ile Met Pro Lys Ala Gly Leu Leu Ile Ile Val Leu Ala Ile Ile
                325                 330                 335
Ala Arg Glu Gly Asp Cys Ala Pro Glu Glu Lys Ile Trp Glu Glu Leu
            340                 345                 350
Ser Val Leu Glu Val Phe Glu Gly Arg Glu Asp Ser Ile Leu Gly Asp
        355                 360                 365
Pro Lys Lys Leu Leu Thr Gln His Phe Val Gln Glu Asn Tyr Leu Glu
    370                 375                 380
Tyr Arg Gln Val Pro Gly Ser Asp Pro Ala Cys Tyr Glu Phe Leu Trp
385                 390                 395                 400
Gly Pro Arg Ala Leu Val Glu Thr Ser Tyr Val Lys Val Leu His His
                405                 410                 415
Met Val Lys Ile Ser Gly Gly Pro His Ile Ser Tyr Pro Pro Leu His
            420                 425                 430
Glu Trp Val Leu Arg Glu Gly Glu Glu Thr Ser Gly Gly His His His
        435                 440                 445
His His His
    450
```

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1353 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

```
ATGGATCCAA AAACTTTAGC CCTTTCTTTA TTAGCAGCTG GCGTACTAGC AGGTTGTAGC     60
AGCCATTCAT CAAATATGGC GAATACCCAA ATGAAATCAG ACAAAATCAT TATTGCTCAC    120
CGTGGTGCTA GCGGTTATTT ACCAGAGCAT ACGTTAGAAT CTAAAGCACT TGCGTTTGCA    180
CAACAGGCTG ATTATTTAGA GCAAGATTTA GCAATGACTA AGGATGGTCG TTTAGTGGTT    240
ATTCACGATC ACTTTTTAGA TGGCTTGACT GATGTTGCGA AAAAATTCCC ACATCGTCAT    300
CGTAAAGATG GCCGTTACTA TGTCATCGAC TTTACCTTAA AAGAAATTCA AAGTTTAGAA    360
ATGACAGAAA ACTTTGAAAC CATGGATCTG GAACAGCGTA GTCAGCACTG CAAGCCTGAA    420
GAAGGCCTTG AGGCCCGAGG AGAGGCCCTG GGCCTGGTGG GTGCGCAGGC TCCTGCTACT    480
GAGGAGCAGG AGGCTGCCTC CTCCTCTTCT ACTCTAGTTG AAGTCACCCT GGGGGAGGTG    540
CCTGCTGCCG AGTCACCAGA TCCTCCCCAG AGTCCTCAGG GAGCCTCCAG CCTCCCCACT    600
ACCATGAACT ACCCTCTCTG GAGCCAATCC TATGAGGACT CCAGCAACCA AGAAGAGGAG    660
GGGCCAAGCA CCTTCCCTGA CCTGGAGTCC GAGTTCCAAG CAGCACTCAG TAGGAAGGTG    720
GCCGAATTGG TTCATTTTCT GCTCCTCAAG TATCGAGCCA GGGAGCCGGT CACAAAGGCA    780
GAAATGCTGG GGAGTGTCGT CGGAAATTGG CAGTATTTCT TTCCTGTGAT CTTCAGCAAA    840
GCTTCCAGTT CCTTGCAGCT GGTCTTTGGC ATCGAGCTGA TGGAAGTGGA CCCCATCGGC    900
CACTTGTACA TCTTTGCCAC CTGCCTGGGC CTCTCCTACG ATGGCCTGCT GGGTGACAAT    960
CAGATCATGC CCAAGGCAGG CCTCCTGATA ATCGTCCTGG CCATAATCGC AAGAGAGGGC   1020
GACTGTGCCC CTGAGGAGAA AATCTGGGAG GAGCTGAGTG TGTTAGAGGT GTTTGAGGGG   1080
AGGGAAGACA GTATCTTGGG GGATCCCAAG AAGCTGCTCA CCCAACATTT CGTGCAGGAA   1140
AACTACCTGG AGTACCGGCA GGTCCCCGGC AGTGATCCTG CATGTTATGA ATTCCTGTGG   1200
GGTCCAAGGG CCCTCGTTGA AACCAGCTAT GTGAAAGTCC TGCACCATAT GGTAAAGATC   1260
AGTGGAGGAC CTCACATTTC CTACCCACCC CTGCATGAGT GGGTTTTGAG AGAGGGGGAA   1320
GAGGGCGGTC ATCACCATCA CCATCACCAT TAA                                1353
```

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1341 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

```
ATGGATCCAA AAACTTTAGC CCTTTCTTTA TTAGCAGCTG GCGTACTAGC AGGTTGTAGC     60
AGCCATTCAT CAAATATGGC GAATACCCAA ATGAAATCAG ACAAAATCAT TATTGCTCAC    120
CGTGGTGCTA GCGGTTATTT ACCAGAGCAT ACGTTAGAAT CTAAAGCACT TGCGTTTGCA    180
CAACAGGCTG ATTATTTAGA GCAAGATTTA GCAATGACTA AGGATGGTCG TTTAGTGGTT    240
ATTCACGATC ACTTTTTAGA TGGCTTGACT GATGTTGCGA AAAAATTCCC ACATCGTCAT    300
CGTAAAGATG GCCGTTACTA TGTCATCGAC TTTACCTTAA AAGAAATTCA AAGTTTAGAA    360
ATGACAGAAA ACTTTGAAAC CATGGGCTCT CTGGAACAGC GTAGTCTGCA CTGCAAGCCT    420
GAGGAAGCCC TTGAGGCCCA ACAAGAGGCC CTGGGCCTGG TGTGTGTGCA GGCTGCCACC    480
TCCTCCTCCT CTCCTCTGGT CCTGGGCACC CTGGAGGAGG TGCCCACTGC TGGGTCAACA    540
GATCCTCCCC AGAGTCCTCA GGGAGCCTCC GCCTTTCCCA CTACCATCAA CTTCACTCGA    600
CAGAGGCAAC CCAGTGAGGG TTCCAGCAGC CGTGAAGAGG AGGGGCCAAG CACCTCTTGT    660
ATCCTGGAGT CCTTGTTCCG AGCAGTAATC ACTAAGAAGG TGGCTGATTT GGTTGGTTTT    720
CTGCTCCTCA AATATCGAGC CAGGGAGCCA GTCACAAAGG CAGAAATGCT GGAGAGTGTC    780
ATCAAAAATT ACAAGCACTG TTTTCCTGAG ATCTTCGGCA AAGCCTCTGA GTCCTTGCAG    840
CTGGTCTTTG GCATTGACGT GAAGGAAGCA GACCCCACCG GCCACTCCTA TGTCCTTGTC    900
ACCTGCCTAG GTCTCTCCTA TGATGGCCTG CTGGGTGATA ATCAGATCAT GCCCAAGACA    960
GGCTTCCTGA TAATTGTCCT GGTCATGATT GCAATGGAGG GCGGCCATGC TCCTGAGGAG   1020
GAAATCTGGG AGGAGCTGAG TGTGATGGAG GTGTATGATG GGAGGGAGCA CAGTGCCTAT   1080
GGGGAGCCCA GGAAGCTGCT CACCCAAGAT TTGGTGCAGG AAAAGTACCT GGAGTACCGG   1140
CAGGTGCCGG ACAGTGATCC CGCACGCTAT GAGTTCCTGT GGGGTCCAAG GGCCCTCGCT   1200
GAAACCAGCT ATGTGAAAGT CCTTGAGTAT GTGATCAAGG TCAGTGCAAG AGTTCGCTTT   1260
TTCTTCCCAT CCCTGCGTGA AGCAGCTTTG AGAGAGGAGG AAGAGGGAGT CGGCGGTCAT   1320
CACCATCACC ATCACCATTA A                                             1341
```

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 466 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```
Met Asp Pro Lys Thr Leu Ala Leu Ser Leu Leu Ala Ala Gly Val Leu
 1               5                  10                  15
Ala Gly Cys Ser Ser His Ser Ser Asn Met Ala Asn Thr Gln Met Lys
            20                  25                  30
Ser Asp Lys Ile Ile Ile Ala His Arg Gly Ala Ser Gly Tyr Leu Pro
        35                  40                  45
Glu His Thr Leu Glu Ser Lys Ala Leu Ala Phe Ala Gln Gln Ala Asp
    50                  55                  60
Tyr Leu Glu Gln Asp Leu Ala Met Thr Lys Asp Gly Arg Leu Val Val
65                  70                  75                  80
Ile His Asp His Phe Leu Asp Gly Leu Thr Asp Val Ala Lys Lys Phe
                85                  90                  95
Pro His Arg His Arg Lys Asp Gly Arg Tyr Tyr Val Ile Asp Phe Thr
            100                 105                 110
Leu Lys Glu Ile Gln Ser Leu Glu Met Thr Glu Asn Phe Glu Thr Met
        115                 120                 125
Gly Ser Leu Glu Gln Arg Ser Leu His Cys Lys Pro Glu Glu Ala Leu
    130                 135                 140
Glu Ala Gln Gln Glu Ala Leu Gly Leu Val Cys Val Gln Ala Ala Thr
145                 150                 155                 160
Ser Ser Ser Ser Pro Leu Val Leu Gly Thr Leu Glu Glu Val Pro Thr
                165                 170                 175
Ala Gly Ser Thr Asp Pro Pro Gln Ser Pro Gln Gly Ala Ser Ala Phe
            180                 185                 190
Pro Thr Thr Ile Asn Phe Thr Arg Gln Arg Gln Pro Ser Glu Gly Ser
        195                 200                 205
Ser Ser Arg Glu Glu Glu Gly Pro Ser Thr Ser Cys Ile Leu Glu Ser
    210                 215                 220
Leu Phe Arg Ala Val Ile Thr Lys Lys Val Ala Asp Leu Val Gly Phe
225                 230                 235                 240
Leu Leu Leu Lys Tyr Arg Ala Arg Glu Pro Val Thr Lys Ala Glu Met
                245                 250                 255
Leu Glu Ser Val Ile Lys Asn Tyr Lys His Cys Phe Pro Glu Ile Phe
            260                 265                 270
Gly Lys Ala Ser Glu Ser Leu Gln Leu Val Phe Gly Ile Asp Val Lys
        275                 280                 285
Glu Ala Asp Pro Thr Gly His Ser Tyr Val Leu Val Thr Cys Leu Gly
    290                 295                 300
Leu Ser Tyr Asp Gly Leu Leu Gly Asp Asn Gln Ile Met Pro Lys Thr
305                 310                 315                 320
Gly Phe Leu Ile Ile Val Leu Val Met Ile Ala Met Glu Gly Gly His
                325                 330                 335
Ala Pro Glu Glu Glu Ile Trp Glu Glu Leu Ser Val Met Glu Val Tyr
            340                 345                 350
Asp Gly Arg Glu His Ser Ala Tyr Gly Glu Pro Arg Lys Leu Leu Thr
        355                 360                 365
Gln Asp Leu Val Gln Glu Lys Tyr Leu Glu Tyr Arg Gln Val Pro Asp
    370                 375                 380
Ser Asp Pro Ala Arg Tyr Glu Phe Leu Trp Gly Pro Arg Ala Leu Ala
385                 390                 395                 400
Glu Thr Ser Tyr Val Lys Val Leu Glu Tyr Val Ile Lys Val Ser Ala
                405                 410                 415
Arg Val Arg Phe Phe Phe Pro Ser Leu Arg Glu Ala Ala Leu Arg Glu
            420                 425                 430
```

```
Glu Glu Glu Gly Val Gly Gly His His His His His His His
        435                 440                 445

          (2) INFORMATION FOR SEQ ID NO:5:

        (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 404 amino acids
          (B) TYPE: amino acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Met Asp Pro Asn Thr Val Ser Ser Phe Gln Val Asp Cys Phe Leu Trp
 1               5                  10                  15
His Val Arg Lys Arg Val Ala Asp Gln Glu Leu Gly Asp Ala Pro Phe
            20                  25                  30
Leu Asp Arg Leu Arg Arg Asp Gln Lys Ser Leu Arg Gly Arg Gly Ser
        35                  40                  45
Thr Leu Gly Leu Asp Ile Glu Thr Ala Thr Arg Ala Gly Lys Gln Ile
    50                  55                  60
Val Glu Arg Ile Leu Lys Glu Glu Ser Asp Glu Ala Leu Lys Met Thr
65                  70                  75                  80
Met Asp Leu Glu Gln Arg Ser Gln His Cys Lys Pro Glu Glu Gly Leu
                85                  90                  95
Glu Ala Arg Gly Glu Ala Leu Gly Leu Val Gly Ala Gln Ala Pro Ala
            100                 105                 110
Thr Glu Glu Gln Glu Ala Ala Ser Ser Ser Ser Thr Leu Val Glu Val
        115                 120                 125
Thr Leu Gly Glu Val Pro Ala Ala Glu Ser Pro Asp Pro Pro Gln Ser
    130                 135                 140
Pro Gln Gly Ala Ser Ser Leu Pro Thr Thr Met Asn Tyr Pro Leu Trp
145                 150                 155                 160
Ser Gln Ser Tyr Glu Asp Ser Ser Asn Gln Glu Glu Glu Gly Pro Ser
                165                 170                 175
Thr Phe Pro Asp Leu Glu Ser Glu Phe Gln Ala Ala Leu Ser Arg Lys
            180                 185                 190
Val Ala Glu Leu Val His Phe Leu Leu Leu Lys Tyr Arg Ala Arg Glu
        195                 200                 205
Pro Val Thr Lys Ala Glu Met Leu Gly Ser Val Val Gly Asn Trp Gln
    210                 215                 220
Tyr Phe Phe Pro Val Ile Phe Ser Lys Ala Ser Ser Ser Leu Gln Leu
225                 230                 235                 240
Val Phe Gly Ile Glu Leu Met Glu Val Asp Pro Ile Gly His Leu Tyr
                245                 250                 255
Ile Phe Ala Thr Cys Leu Gly Leu Ser Tyr Asp Gly Leu Leu Gly Asp
            260                 265                 270
Asn Gln Ile Met Pro Lys Ala Gly Leu Leu Ile Ile Val Leu Ala Ile
        275                 280                 285
Ile Ala Arg Glu Gly Asp Cys Ala Pro Glu Glu Lys Ile Trp Glu Glu
    290                 295                 300
Leu Ser Val Leu Glu Val Phe Glu Gly Arg Glu Asp Ser Ile Leu Gly
305                 310                 315                 320
Asp Pro Lys Lys Leu Leu Thr Gln His Phe Val Gln Glu Asn Tyr Leu
                325                 330                 335
Glu Tyr Arg Gln Val Pro Gly Ser Asp Pro Ala Cys Tyr Glu Phe Leu
            340                 345                 350
Trp Gly Pro Arg Ala Leu Val Glu Thr Ser Tyr Val Lys Val Leu His
        355                 360                 365
His Met Val Lys Ile Ser Gly Gly Pro His Ile Ser Tyr Pro Pro Leu
    370                 375                 380
His Glu Trp Val Leu Arg Glu Gly Glu Glu Gly Gly His His His His
```

385 390 395 400
His His His

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1212 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

ATGGATCCAA ACACTGTGTC AAGCTTTCAG GTAGATTGCT TTCTTTGGCA TGTCCGCAAA 60
CGAGTTGCAG ACCAAGAACT AGGTGATGCC CCATTCCTTG ATCGGCTTCG CCGAGATCAG 120
AAATCCCTAA GAGGAAGGGG CAGCACTCTT GGTCTGGACA TCGAGACAGC CACACGTGCT 180
GGAAAGCAGA TAGTGGAGCG GATTCTGAAA GAAGAATCCG ATGAGGCACT TAAAATGACC 240
ATGGATCTGG AACAGCGTAG TCAGCACTGC AAGCCTGAAG AAGGCCTTGA GGCCCGAGGA 300
GAGGCCCTGG GCCTGGTGGG TGCGCAGGCT CCTGCTACTG AGGAGCAGGA GGCTGCCTCC 360
TCCTCTTCTA CTCTAGTTGA AGTCACCCTG GGGGAGGTGC CTGCTGCCGA GTCACCAGAT 420
CCTCCCCAGA GTCCTCAGGG AGCCTCCAGC CTCCCCACTA CCATGAACTA CCCTCTCTGG 480
AGCCAATCCT ATGAGGACTC CAGCAACCAA GAAGAGGAGG GGCCAAGCAC CTTCCCTGAC 540
CTGGAGTCCG AGTTCCAAGC AGCACTCAGT AGGAAGGTGG CCGAATTGGT TCATTTTCTG 600
CTCCTCAAGT ATCGAGCCAG GGAGCCGGTC ACAAAGGCAG AAATGCTGGG GAGTGTCGTC 660
GGAAATTGGC AGTATTTCTT TCCTGTGATC TTCAGCAAAG CTTCCAGTTC CTTGCAGCTG 720
GTCTTTGGCA TCGAGCTGAT GGAAGTGGAC CCCATCGGCC ACTTGTACAT CTTTGCCACC 780
TGCCTGGGCC TCTCCTACGA TGGCCTGCTG GGTGACAATC AGATCATGCC CAAGGCAGGC 840
CTCCTGATAA TCGTCCTGGC CATAATCGCA AGAGAGGGCG ACTGTGCCCC TGAGGAGAAA 900
ATCTGGGAGG AGCTGAGTGT GTTAGAGGTG TTTGAGGGGA GGGAAGACAG TATCTTGGGG 960
GATCCCAAGA AGCTGCTCAC CCAACATTTC GTGCAGGAAA ACTACCTGGA GTACCGGCAG 1020
GTCCCCGGCA GTGATCCTGC ATGTTATGAA TTCCTGTGGG GTCCAAGGGC CCTCGTTGAA 1080
ACCAGCTATG TGAAAGTCCT GCACCATATG GTAAAGATCA GTGGAGGACC TCACATTTCC 1140
TACCCACCCC TGCATGAGTG GGTTTTGAGA GAGGGGGAAG AGGGCGGTCA TCACCATCAC 1200
CATCACCATT AA 1212

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 445 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

Met Lys Gly Gly Ile Val His Ser Asp Gly Ser Tyr Pro Lys Asp Lys
1 5 10 15
Phe Glu Lys Ile Asn Gly Thr Trp Tyr Tyr Phe Asp Ser Ser Gly Tyr
20 25 30
Met Leu Ala Asp Arg Trp Arg Lys His Thr Asp Gly Asn Trp Tyr Trp
35 40 45
Phe Asp Asn Ser Gly Glu Met Ala Thr Gly Trp Lys Lys Ile Ala Asp
50 55 60
Lys Trp Tyr Tyr Phe Asn Glu Glu Gly Ala Met Lys Thr Gly Trp Val
65 70 75 80
Lys Tyr Lys Asp Thr Trp Tyr Tyr Leu Asp Ala Lys Glu Gly Ala Met
85 90 95
Val Ser Asn Ala Phe Ile Gln Ser Ala Asp Gly Thr Gly Trp Tyr Tyr
100 105 110

```
Leu Lys Pro Asp Gly Thr Leu Ala Asp Arg Pro Glu Leu Asp Met Gly
        115                 120                 125
Ser Leu Glu Gln Arg Ser Leu His Cys Lys Pro Glu Glu Ala Leu Glu
    130                 135                 140
Ala Gln Gln Glu Ala Leu Gly Leu Val Cys Val Gln Ala Ala Thr Ser
145                 150                 155                 160
Ser Ser Ser Pro Leu Val Leu Gly Thr Leu Glu Glu Val Pro Thr Ala
                165                 170                 175
Gly Ser Thr Asp Pro Pro Gln Ser Pro Gln Gly Ala Ser Ala Phe Pro
            180                 185                 190
Thr Thr Ile Asn Phe Thr Arg Gln Arg Gln Pro Ser Glu Gly Ser Ser
        195                 200                 205
Ser Arg Glu Glu Glu Gly Pro Ser Thr Ser Cys Ile Leu Glu Ser Leu
    210                 215                 220
Phe Arg Ala Val Ile Thr Lys Lys Val Ala Asp Leu Val Gly Phe Leu
225                 230                 235                 240
Leu Leu Lys Tyr Arg Ala Arg Glu Pro Val Thr Lys Ala Glu Met Leu
                245                 250                 255
Glu Ser Val Ile Lys Asn Tyr Lys His Cys Phe Pro Glu Ile Phe Gly
            260                 265                 270
Lys Ala Ser Glu Ser Leu Gln Leu Val Phe Gly Ile Asp Val Lys Glu
        275                 280                 285
Ala Asp Pro Thr Gly His Ser Tyr Val Leu Val Thr Cys Leu Gly Leu
    290                 295                 300
Ser Tyr Asp Gly Leu Leu Gly Asp Asn Gln Ile Met Pro Lys Thr Gly
305                 310                 315                 320
Phe Leu Ile Ile Val Leu Val Met Ile Ala Met Glu Gly Gly His Ala
                325                 330                 335
Pro Glu Glu Glu Ile Trp Glu Glu Leu Ser Val Met Glu Val Tyr Asp
            340                 345                 350
Gly Arg Glu His Ser Ala Tyr Gly Glu Pro Arg Lys Leu Leu Thr Gln
        355                 360                 365
Asp Leu Val Gln Glu Lys Tyr Leu Glu Tyr Arg Gln Val Pro Asp Ser
    370                 375                 380
Asp Pro Ala Arg Tyr Glu Phe Leu Trp Gly Pro Arg Ala Leu Ala Glu
385                 390                 395                 400
Thr Ser Tyr Val Lys Val Leu Glu Tyr Val Ile Lys Val Ser Ala Arg
                405                 410                 415
Val Arg Phe Phe Phe Pro Ser Leu Arg Glu Ala Ala Leu Arg Glu Glu
            420                 425                 430
Glu Glu Gly Val Gly Gly His His His His His His
        435                 440                 445
```

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1338 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

```
ATGAAAGGGG GAATTGTACA TTCAGACGGC TCTTATCCAA AAGACAAGTT TGAGAAAATC      60
AATGGCACTT GGTACTACTT TGACAGTTCA GGCTATATGC TTGCAGACCG CTGGAGGAAG     120
CACACAGACG GCAACTGGTA CTGGTTCGAC AACTCAGGCG AAATGGCTAC AGGCTGGAAG     180
AAAATCGCTG ATAAGTGGTA CTATTTCAAC GAAGAAGGTG CCATGAAGAC AGGCTGGGTC     240
AAGTACAAGG ACACTTGGTA CTACTTAGAC GCTAAAGAAG GCGCCATGGT ATCAAATGCC     300
TTTATCCAGT CAGCGGACGG AACAGGCTGG TACTACCTCA AACCAGACGG AACACTGGCA     360
GACAGGCCAG AATTGGACAT GGGCTCTCTG GAACAGCGTA GTCTGCACTG CAAGCCTGAG     420
GAAGCCCTTG AGGCCCAACA AGAGGCCCTG GGCCTGGTGT GTGTGCAGGC TGCCACCTCC     480
TCCTCCTCTC CTCTGGTCCT GGGCACCCTG GAGGAGGTGC CCACTGCTGG GTCAACAGAT     540
```

```
CCTCCCCAGA GTCCTCAGGG AGCCTCCGCC TTTCCCACTA CCATCAACTT CACTCGACAG    600
AGGCAACCCA GTGAGGGTTC CAGCAGCCGT GAAGAGGAGG GGCCAAGCAC CTCTTGTATC    660
CTGGAGTCCT TGTTCCGAGC AGTAATCACT AAGAAGGTGG CTGATTTGGT TGGTTTTCTG    720
CTCCTCAAAT ATCGAGCCAG GGAGCCAGTC ACAAAGGCAG AAATGCTGGA GAGTGTCATC    780
AAAAATTACA AGCACTGTTT TCCTGAGATC TTCGGCAAAG CCTCTGAGTC CTTGCAGCTG    840
GTCTTTGGCA TTGACGTGAA GGAAGCAGAC CCCACCGGCC ACTCCTATGT CCTTGTCACC    900
TGCCTAGGTC TCTCCTATGA TGGCCTGCTG GGTGATAATC AGATCATGCC CAAGACAGGC    960
TTCCTGATAA TTGTCCTGGT CATGATTGCA ATGGAGGGCG GCCATGCTCC TGAGGAGGAA   1020
ATCTGGGAGG AGCTGAGTGT GATGGAGGTG TATGATGGGA GGGAGCACAG TGCCTATGGG   1080
GAGCCCAGGA AGCTGCTCAC CCAAGATTTG GTGCAGGAAA AGTACCTGGA GTACCGGCAG   1140
GTGCCGGACA GTGATCCCGC ACGCTATGAG TTCCTGTGGG GTCCAAGGGC CCTCGCTGAA   1200
ACCAGCTATG TGAAAGTCCT TGAGTATGTG ATCAAGGTCA GTGCAAGAGT TCGCTTTTTC   1260
TTCCCATCCC TGCGTGAAGC AGCTTTGAGA GAGGAGGAAG AGGGAGTCGG CGGTCATCAC   1320
CATCACCATC ACCATTAA                                                 1338
```

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 454 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

```
Met Lys Gly Gly Ile Val His Ser Asp Gly Ser Tyr Pro Lys Asp Lys
 1               5                  10                  15
Phe Glu Lys Ile Asn Gly Thr Trp Tyr Tyr Phe Asp Ser Ser Gly Tyr
            20                  25                  30
Met Leu Ala Asp Arg Trp Arg Lys His Thr Asp Gly Asn Trp Tyr Trp
        35                  40                  45
Phe Asp Asn Ser Gly Glu Met Ala Thr Gly Trp Lys Lys Ile Ala Asp
    50                  55                  60
Lys Trp Tyr Tyr Phe Asn Glu Glu Gly Ala Met Lys Thr Gly Trp Val
65                  70                  75                  80
Lys Tyr Lys Asp Thr Trp Tyr Tyr Leu Asp Ala Lys Glu Gly Ala Met
                85                  90                  95
Val Ser Asn Ala Phe Ile Gln Ser Ala Asp Gly Thr Gly Trp Tyr Tyr
            100                 105                 110
Leu Lys Pro Asp Gly Thr Leu Ala Asp Arg Pro Glu Leu Ala Ser Met
        115                 120                 125
Leu Asp Met Asp Leu Glu Gln Arg Ser Gln His Cys Lys Pro Glu Glu
    130                 135                 140
Gly Leu Glu Ala Arg Gly Glu Ala Leu Gly Leu Val Gly Ala Gln Ala
145                 150                 155                 160
Pro Ala Thr Glu Glu Gln Glu Ala Ala Ser Ser Ser Ser Thr Leu Val
                165                 170                 175
Glu Val Thr Leu Gly Glu Val Pro Ala Ala Glu Ser Pro Asp Pro Pro
            180                 185                 190
Gln Ser Pro Gln Gly Ala Ser Ser Leu Pro Thr Thr Met Asn Tyr Pro
        195                 200                 205
Leu Trp Ser Gln Ser Tyr Glu Asp Ser Ser Asn Gln Glu Glu Glu Gly
    210                 215                 220
Pro Ser Thr Phe Pro Asp Leu Glu Ser Glu Phe Gln Ala Ala Leu Ser
225                 230                 235                 240
Arg Lys Val Ala Glu Leu Val His Phe Leu Leu Leu Lys Tyr Arg Ala
                245                 250                 255
Arg Glu Pro Val Thr Lys Ala Glu Met Leu Gly Ser Val Val Gly Asn
            260                 265                 270
Trp Gln Tyr Phe Phe Pro Val Ile Phe Ser Lys Ala Ser Ser Ser Leu
        275                 280                 285
Gln Leu Val Phe Gly Ile Glu Leu Met Glu Val Asp Pro Ile Gly His
```

```
    290                 295                 300
Leu Tyr Ile Phe Ala Thr Cys Leu Gly Leu Ser Tyr Asp Gly Leu Leu
305                 310                 315                 320
Gly Asp Asn Gln Ile Met Pro Lys Ala Gly Leu Leu Ile Ile Val Leu
                325                 330                 335
Ala Ile Ile Ala Arg Glu Gly Asp Cys Ala Pro Glu Glu Lys Ile Trp
            340                 345                 350
Glu Glu Leu Ser Val Leu Glu Val Phe Glu Gly Arg Glu Asp Ser Ile
        355                 360                 365
Leu Gly Asp Pro Lys Lys Leu Leu Thr Gln His Phe Val Gln Glu Asn
    370                 375                 380
Tyr Leu Glu Tyr Arg Gln Val Pro Gly Ser Asp Pro Ala Cys Tyr Glu
385                 390                 395                 400
Phe Leu Trp Gly Pro Arg Ala Leu Val Glu Thr Ser Tyr Val Lys Val
                405                 410                 415
Leu His His Met Val Lys Ile Ser Gly Gly Pro His Ile Ser Tyr Pro
            420                 425                 430
Pro Leu His Glu Trp Val Leu Arg Glu Gly Glu Glu Gly Gly His His
        435                 440                 445
His His His His His
    450
```

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1362 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

```
ATGAAAGGGG GAATTGTACA TTCAGACGGC TCTTATCCAA AAGACAAGTT TGAGAAAATC     60
AATGGCACTT GGTACTACTT TGACAGTTCA GGCTATATGC TTGCAGACCG CTGGAGGAAG    120
CACACAGACG GCAACTGGTA CTGGTTCGAC AACTCAGGCG AAATGGCTAC AGGCTGGAAG    180
AAAATCGCTG ATAAGTGGTA CTATTTCAAC GAAGAAGGTG CCATGAAGAC AGGCTGGGTC    240
AAGTACAAGG ACACTTGGTA CTACTTAGAC GCTAAAGAAG GCGCCATGGT ATCAAATGCC    300
TTTATCCAGT CAGCGGACGG AACAGGCTGG TACTACCTCA AACCAGACGG AACACTGGCA    360
GACAGGCCAG AATTGGCCAG CATGCTGGAC ATGGATCTGG AACAGCGTAG TCAGCACTGC    420
AAGCCTGAAG AAGGCCTTGA GGCCCGAGGA GAGGCCCTGG GCCTGGTGGG TGCGCAGGCT    480
CCTGCTACTG AGGAGCAGGA GGCTGCCTCC TCCTCTTCTA CTCTAGTTGA AGTCACCCTG    540
GGGGAGGTGC CTGCTGCCGA GTCACCAGAT CCTCCCCAGA GTCCTCAGGG AGCCTCCAGC    600
CTCCCCACTA CCATGAACTA CCCTCTCTGG AGCCAATCCT ATGAGGACTC CAGCAACCAA    660
GAAGAGGAGG GGCCAAGCAC CTTCCCTGAC CTGGAGTCTG AGTTCCAAGC AGCACTCAGT    720
AGGAAGGTGG CCAAGTTGGT TCATTTTCTG CTCCTCAAGT ATCGAGCCAG GGAGCCGGTC    780
ACAAAGGCAG AAATGCTGGG GAGTGTCGTC GGAAATTGGC AGTACTTCTT TCCTGTGATC    840
TTCAGCAAAG CTTCCGATTC CTTGCAGCTG GTCTTTGGCA TCGAGCTGAT GGAAGTGGAC    900
CCCATCGGCC ACGTGTACAT CTTTGCCACC TGCCTGGGCC TCTCCTACGA TGGCCTGCTG    960
GGTGACAATC AGATCATGCC CAAGACAGGC TTCCTGATAA TCATCCTGGC CATAATCGCA   1020
AAAGAGGGCG ACTGTGCCCC TGAGGAGAAA ATCTGGGAGG AGCTGAGTGT GTTAGAGGTG   1080
TTTGAGGGGA GGGAAGACAG TATCTTCGGG GATCCCAAGA AGCTGCTCAC CCAATATTTC   1140
GTGCAGGAAA ACTACCTGGA GTACCGGCAG GTCCCCGGCA GTGATCCTGC ATGCTATGAG   1200
TTCCTGTGGG GTCCAAGGGC CCTCATTGAA ACCAGCTATG TGAAAGTCCT GCACCATATG   1260
GTAAAGATCA GTGGAGGACC TCGCATTTCC TACCCACTCC TGCATGAGTG GGCTTTGAGA   1320
GAGGGGGAAG AGGGCGGTCA TCACCATCAC CATCACCATT AA                      1362
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